

**Amendments to the Claims**

Please cancel Claims 1-27, 42-55, 65-75, 84, 93, 94, 102, 103, 105-109, 111 and 116-130. Please add new Claims 158-166. Please amend Claims 28, 56, 132, 134-136 and 148. The Claim Listing below will replace all prior versions of the claims in the application:

**Claim Listing**

1-27. (Canceled)

28. (Currently Amended) A method of identifying an agent that alters NAD-dependent deacetylation activity of a Sir2 protein, comprising the step of measuring NAD-dependent deacetylation activity of a Sir2 protein or a fragment of the Sir2 protein with respect to at least one lysine residue in an acetylated protein in the presence of the agent, wherein the fragment of the Sir2 protein comprises a core domain of Sir2 and includes ~~an~~ at least one amino acid sequence selected from the group consisting of the amino acid sequence ~~represented in at least one of Figs. 2C, 6A, 14A and 19; and SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 27 and SEQ ID NO: 28 and SEQ ID NO: 38.~~

29. (Original) The method of Claim 28, wherein the acetylated protein is a nuclear protein.

30. (Original) The method of Claim 29, wherein the nuclear protein is a histone protein.

31. (Original) The method of Claim 28, wherein the acetylated protein is a cytoplasmic protein.

32.-55. (Canceled)

56. (Currently Amended) A method of identifying an agent that alters NAD-dependent deacetylation activity of a Sir2 protein, comprising the steps of:

- a) combining an acetylated protein, the agent to be tested and the Sir2 protein or a fragment of the Sir2 protein, wherein the fragment of the Sir2 protein comprises a core domain of Sir2 and includes ~~an~~ at least one amino acid sequence selected from the group consisting of the amino acid sequence ~~represented in at least one~~ of Figs. 2C, 6A, 14A ~~and 19~~; and SEQ ID NO: ~~2~~, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 27 ~~and~~ ,SEQ ID NO: 28 ~~and~~ SEQ ID NO: 38;
- b) measuring NAD-dependent deacetylation activity of the Sir2 protein or the fragment of the Sir2 protein with respect to at least one lysine residue in the acetylated protein; and
- c) comparing the NAD-dependent deacetylation activity of the Sir2 protein or the fragment of the Sir2 protein with respect to at least one lysine residue in the acetylated protein in the presence of the agent with the NAD-dependent deacetylation activity of the Sir2 protein or the fragment of the Sir2 protein with respect to at least one lysine residue in the acetylated protein in the absence of the agent,

wherein a difference in the NAD-dependent deacetylation activity of the Sir2 protein or the fragment of the Sir2 protein with respect to at least one lysine residue in the acetylated protein in the presence of the agent identifies the agent that alters NAD-dependent deacetylation of the Sir2 protein.

57.-59. (Canceled)

- 60. (Previously Presented) The method of Claim 56, wherein the acetylated protein is a nuclear protein.
- 61. (Original) The method according to Claim 60, wherein the nuclear protein is a histone protein.

62. (Previously Presented) The method of Claim 56, wherein the acetylated protein is a cytoplasmic protein.
63. (Canceled)
64. (Previously Presented) The method according to Claim 56, wherein the Sir2 protein is a Sir2a protein.
- 65.-130. (Cancelled)
131. (Previously Presented) The method of Claim 28, wherein the Sir2 protein is an isolated Sir2 protein.
132. (Currently Amended) The method of Claim 131, wherein the isolated Sir2 protein comprises ~~includes~~ a recombinant Sir2 protein.
133. (Previously Presented) The method of Claim 56, wherein the Sir2 protein is an isolated Sir2 protein.
134. (Currently Amended) The method of Claim 133, wherein the isolated Sir2 protein comprises ~~includes~~ a recombinant Sir2 protein.
135. (Currently Amended) The method of Claim 28, wherein the Sir2 protein comprises ~~includes~~ a human Sir2 protein.
136. (Currently Amended) The method of Claim 56, wherein the Sir2 protein comprises ~~includes~~ a human Sir2 protein.
- 137.-138. (Canceled)
139. (Previously Presented) The method of Claim 28, wherein the Sir2 protein is a nuclear protein.
140. (Previously Presented) The method of Claim 56, wherein the Sir2 protein is a nuclear protein.

141. (Previously Presented) The method of Claim 28, wherein a decrease in NAD-dependent deacetylation activity of the Sir2 protein with respect to at least one lysine residue in the acetylated protein in the presence of the agent compared to the NAD-dependent deacetylation activity of the Sir2 protein with respect to at least one lysine residue in the acetylated protein in the absence of the agent indicates the agent decreases NAD-dependent deacetylation activity of the Sir2 protein.
142. (Previously Presented) The method of Claim 141, wherein the agent is an antagonist of NAD-dependent deacetylation activity of the Sir2 protein.
143. (Previously Presented) The method of Claim 28, wherein an increase in NAD-dependent deacetylation activity of the Sir2 protein with respect to at least one lysine residue in the acetylated protein in the presence of the agent compared to the NAD-dependent deacetylation activity of the Sir2 protein with respect to at least one lysine residue in the acetylated protein in the absence of the agent indicates the agent increases NAD-dependent deacetylation activity of the Sir2 protein.
144. (Previously Presented) The method of Claim 143, wherein the agent is an agonist of NAD-dependent deacetylation activity of the Sir2 protein.
145. (Previously Presented) The method of Claim 56, wherein the difference in NAD-dependent deacetylation activity of the Sir2 protein or the fragment of the Sir2 protein is an increase in NAD-dependent deacetylation activity and identifies the agent that increases NAD-dependent deacetylation activity of the Sir2 protein.
146. (Previously Presented) The method of Claim 145, wherein the agent is an agonist of NAD-dependent deacetylation activity of the Sir2 protein.
147. (Previously Presented) The method of Claim 56, wherein the difference in NAD-dependent deacetylation activity of the Sir2 protein or the fragment of the Sir2 protein is a decrease in NAD-dependent deacetylation activity and identifies the agent that decreases NAD-dependent deacetylation activity.

- 148. (Currently Amended) The method of Claim 147 146, wherein the agent is an antagonist of NAD-dependent deacetylation activity of the Sir2 protein.
- 149. (Not Entered)
- 150. (Not Entered)
- 151. (Not Entered)
- 152. (Not Entered)
- 153. (Not Entered)
- 154. (Not Entered)
- 155. (Not Entered)
- 156. (Not Entered)
- 157. (Not Entered)
- 158. (New) The method of Claim 28, wherein the Sir2 protein is a Sir2 $\alpha$  protein.
- 159. (New) The method of Claim 149, wherein the Sir2 $\alpha$  protein comprises the amino acid sequence of SEQ ID NO: 1.
- 160. (New) The method of Claim 28, wherein the fragment of the Sir2 protein comprises the amino acid sequence of SEQ ID NO: 9.
- 161. (New) The method of Claim 28, wherein the fragment of the Sir2 protein comprises the amino acid sequence of SEQ ID NO: 19.
- 162. (New) The method of Claim 28, wherein the fragment of the Sir2 protein comprises the amino acid sequence of SEQ ID NO: 38.

163. (New) The method of Claim 64, wherein the Sir2 $\alpha$  protein comprises the amino acid sequence of SEQ ID NO: 1.
164. (New) The method of Claim 56, wherein the fragment of the Sir2 protein comprises the amino acid sequence of SEQ ID NO: 9.
165. (New) The method of Claim 56, wherein the fragment of the Sir2 protein comprises the amino acid sequence of SEQ ID NO: 19.
166. (New) The method of Claim 56, wherein the fragment of the Sir2 protein comprises the amino acid sequence of SEQ ID NO: 38.